

clearly teach that ultrasonic energy has been used to disrupt cells but without the exclusion of beads."

However, it is respectfully submitted that there are significant differences between the disclosures of the cited references and the claimed invention.

Specifically, Miller discloses a device for ultrasonic inspection of "flat and curved structures relative to joint defects, cracks, far side surface corrosion and material delaminations" (column 3, lines 30-35). In contrast, the claimed invention relates to a method for disrupting cells, including providing a sonic bath including a first liquid, placing into the first liquid a vessel including cells in a second liquid, and subjecting the cells to ultrasonic energy. Miller does not disclose: disruption of cells; a sonic bath with a first liquid; placing into the first liquid a vessel including cells in a second liquid; or subjecting cells to ultrasonic energy. Miller uses ultrasonic energy in a completely different way for a completely different purpose than the claimed invention.

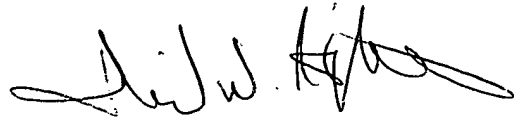
Furthermore, the disclosure of Wood et al. does not provide much additional relevant information. It is alleged that Wood et al., at columns 6-7, all lines, teach the use of a sonic bath to lyse mycobacteria. The Applicants can not find this teaching. The Applicants found four references to sonication in Wood et al.:

- (1) Example 2a, third paragraph (column 6) – "Monoclonal antibodies against irradiated *M. bovis* sonicate, were raised ... characterized ....(Wood et.al, 1988)". However, this reference to a sonicate fails to teach any particular sonication method, or whether sonication causes disruption of cells.
- (2) Example 3a, third to fourth paragraph (column 8) – "DNA extraction was essentially by the method of Shoemaker et.al. (1986). Construction of the *M. bovis* library in lambda.gt11. *M. bovis* DNA was sonicated briefly ... giving DNA fragments ranging in size from 2kb to 200bp ...." However, in this Example, it is DNA which is subjected to sonication, rather than cells as in the claimed method. Furthermore, the method of Shoemaker (which was used for extraction of the DNA) utilizes a mixture of lysozyme, SDS detergent, and Proteinase K to lyse the cells, not sonication.

- (3) Example 3b (column 10) - "Construction of a .lambda.gt11 library of M. bovis. M. bovis AN5 DNA was extracted, sonicated and cloned into lambda.gt11." As in Example 3a, above, it is the extracted DNA which is subjected to sonication rather than cells. Also, it is presumed that the method of Shoemaker was used for extraction here as well.
- (4) Example 5a (column 12) - "The mycobacteria listed were cultured ... and harvested by centrifugation. Cell pellets were heat-killed .... The cell suspensions were sonicated for 5 seconds on ice. Proteinase K was added to give a final concentration of 60ug/ml and the suspensions were incubated at 65°C for 1 hour." As with the reference to a sonicate in Example 2a, this reference to sonication fails to teach any particular sonication method. Also, the short time of sonication (5 seconds) and the use of Proteinase K suggest that it is not sonication which causes disruption of cells as in the claimed invention.

In view of the lack of teaching in the cited references which is relevant to the claimed invention, reconsideration and withdrawal of the claim rejections is requested.

Respectfully submitted,



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